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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,722	04/19/2000	DAVID J SQUIRRELL	124-765	3335
23117	7590	10/23/2006	EXAMINER	
NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203			STEADMAN, DAVID J	
			ART UNIT	PAPER NUMBER

1656

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/529,722

Applicant(s)

SQUIRRELL ET AL.

Examiner

David J. Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 107-135 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 107-135 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☒ Other: Appendix A.

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6 January 2006 has been entered.

[2] Claims 107-135 are pending in the application.

[3] Applicant's arguments filed 6 January 2006 have been fully considered.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objection(s)

[5] The objection to claims 117 and 125 in the recitation of "anenylylate kinase" is maintained for the reasons of record. In the response filed 6 January 2006, applicant fails to acknowledge or respond to the instant objection. As noted in the prior Office action, it is suggested that applicant replace "anenylylate" in claims 117 and 125 with "adenylylate."

Claim Rejections - 35 USC § 112, Second Paragraph

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[6] The rejection of claims 108-109, 111, 115-116, 120-135 as being indefinite in the recitation of "Photinus pyralis luciferase which has a mutation at position 354," "Luciola luciferase with a mutation at position 354," "Luciola luciferase in which the amino acid at the 217 position," and "amino acid 87 or 107 in the sequence of *E. coli* adenylate kinase" is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicant argues the examiner's concern is based on a hypothetical as the examiner has failed to present any evidence that the numbering recited in the claims would not be definite.

Applicant's argument is not found persuasive. As noted in the prior Office action, a skilled artisan recognizes that identifying a specific amino acid by position number depends upon the reference sequence. Put another way, the numbering of an amino acid position within a polypeptide sequence is relative to the intended reference sequence. According to applicant, the sequences of Photinus pyralis luciferase, *Luciola* luciferases, and *E. coli* adenylate kinase are well known and there is no ambiguity in these sequences. However, for reasons that follow, a skilled artisan would recognize that the amino acid at a particular position within a polypeptide sequence is variable. Using *E. coli* adenylate kinase as a representative example, it is noted that Liang et al. (cited in the PTO-892 of the Office action mailed on 7 November 2000) discloses that position 107 of *E. coli* adenylate kinase is a leucine. Also, Gilles et al. (cited in the PTO-892 of the Office action mailed on 24 January 2002) discloses that position 87 of *E. coli* adenylate kinase is proline. However, the *E. coli* adenylate kinase polypeptide as disclosed by GenBank Accession Number BAA14303 discloses alanine and glycine at

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residues 87 and 107, respectively. According to MPEP 2173.05(b), "[a] claim may be rendered indefinite by reference to an object that is variable." Because the sequence of a polypeptide referred to as, e.g., *E. coli* adenylate kinase, varies in the prior art, the terms "Photinus pyralis luciferase which has a mutation at position 354," "Luciola luciferase with a mutation at position 354," "Luciola luciferase in which the amino acid at the 217 position," and "amino acid 87 or 107 in the sequence of *E. coli* adenylate kinase" are indefinite.

[7] The rejection of claim 127 as being indefinite in the recitation of "particular different antibiotic resistance genes" is maintained. In the response filed 6 January 2006, applicant fails to acknowledge or respond to the instant rejection and thus the rejection is maintained for the reasons of record and the reasons stated below.

Claim Rejections - 35 USC § 112, First Paragraph

[8] The new matter rejection of claims 117-119, 125-127, and 133-135 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action (6 October 2005 Office action at paragraph 11).

RESPONSE TO ARGUMENT: Applicant argues specific support for the claim amendments at issue can be found in the prior art, e.g., European Application No. 92110808.0, which is referred to in the application. Applicant argues one should not be required to re-teach what was known in the art.

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Applicant's argument is not found persuasive. MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description." The examiner acknowledges the specification's reference to European Application No. 92110808.0 (specification at p. 8, line 21). According to MPEP § 608.01(p), incorporation by reference of material in a non-patent document "must be set forth in the specification and must: (1) Express a clear intent to incorporate by reference by using the root words "incorporat(e)" and "reference" (e.g., "incorporate by reference"); and (2) Clearly identify the referenced patent, application, or publication." See 37 § 1.57(b). MPEP § 608.01(p) further states, "[i]f a reference to a document does not clearly indicate an intended incorporation by reference, examination will proceed as if no incorporation by reference statement has been made and the Office will not expend resources trying to determine if an incorporation by reference was intended." It is noted that there is no clear intent to incorporate by reference material from European Application No. 92110808.0 using the root words "incorporat(e)" and "reference" (e.g., "incorporate by reference"). Thus, according to MPEP § 608.01(p), "examination will proceed as if no incorporation by reference statement has been made." As such, the examiner considers the claim amendment filed 5 August 2005 to introduce new matter.

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[9] The new matter rejection of claims 108-109, 115-116, and 120-135 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action (5 May 2005 Office action at paragraph 14).

RESPONSE TO ARGUMENT: Applicant argues specific support for the claim amendments at issue can be found in the prior art, *e.g.*, European Application No. 92110808.0, which is referred to in the application. Applicant argues one should not be required to re-teach what was known in the art.

Applicant's argument is not found persuasive. MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description." The examiner acknowledges the specification's reference to European Application No. 92110808.0 (specification at p. 8, line 21). According to MPEP § 608.01(p), incorporation by reference of material in a non-patent document "must be set forth in the specification and must: (1) Express a clear intent to incorporate by reference by using the root words "incorporat(e)" and "reference" (*e.g.*, "incorporate by reference"); and (2) Clearly identify the referenced patent, application, or publication." See 37 § 1.57(b). MPEP § 608.01(p) further states, "[i]f a reference to a document does not clearly indicate an intended incorporation by reference, examination will proceed as if no incorporation by reference statement has been made and the

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Office will not expend resources trying to determine if an incorporation by reference was intended." It is noted that there is no clear intent to incorporate by reference material from European Application No. 92110808.0 using the root words "incorporat(e)" and "reference" (e.g., "incorporate by reference"). Thus, according to MPEP § 608.01(p), "examination will proceed as if no incorporation by reference statement has been made." As such, the examiner considers the claim amendment filed 5 August 2005 to introduce new matter.

[10] The written description rejection of claims 107-135 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action (5 May 2005 Office action at paragraph 15).

RESPONSE TO ARGUMENT: Applicant argues that in view of the prior art of record, one of skill in the art will appreciate that luciferases share a common related structure as well as function.

Applicant's argument is not found persuasive. The examiner maintains the position that the genus of mutant luciferase and mutant adenylate kinases are not adequately described in the specification. In this case, the genus of luciferase and adenylate kinase polypeptides and corresponding encoding nucleic acids as recited in the claims are not so limited to those of the prior art. Instead, each genus, with the exception of a single amino acid substitution in certain of the claims, is not limited to having any common structural feature(s). In this case, the luciferase species disclosed

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in European Patent Application No. 92 1 10808.0 and WO 95/25798 and adenylate kinase species disclosed by Liang et al. and Gilles et al. fail to reflect the structural variation among the members of the genus, which encompasses species that are widely variant with respect to their structures. Given the lack of description of a representative number of species, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[11] The scope of enablement rejection of claims 107-135 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action (5 May 2005 Office action at paragraph 16).

RESPONSE TO ARGUMENT: Applicant argues a skilled artisan would not be required to alter every amino acid to make and use the claimed invention. According to applicant, it is more likely that a skilled artisan would make a luciferase with some alterations and the specification provides guidance for determining whether the proteins would be useful in accordance with the claimed invention.

Applicant's argument is not found persuasive. The examiner maintains the position that the specification, even in view of the teachings of the prior art, fails to enable the full scope of the claimed invention without undue experimentation.

According to applicant, it appears that the specification, in view of the teachings of the prior art, would enable a skilled artisan to make any thermostable luciferase

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polypeptide/encoding nucleic acid as encompassed by the claims. The claims are so broad as to essentially encompass the use of any mutant luciferase or adenylate kinase that has the required activity as recited in the claims. While applicant argues that a skilled artisan is required to make only "some" variations within the sequence, it is noted that the claims encompass any amino acid mutation(s) and the specification should enable the full scope of the claim, not just those variants having "some" amino acid alterations, which applicant argues are enabled by the specification. However, neither the specification nor the prior art nor the combination thereof provides the necessary guidance to make all luciferase and adenylate kinase variants as encompassed by the claims and there was a high level of unpredictability in the art in altering the amino acid sequence of a protein to achieve a desired activity, which is undisputed by applicant. While the examiner acknowledges that the specification and prior art disclose screening methods for determining whether the mutant luciferase or mutant adenylate kinase polypeptides are useful in accordance with the claimed invention, it was not routine in the art at the time of the invention to make all luciferase and adenylate kinase variants, having essentially any alterations that achieve the desired activity/utility as broadly encompassed by the claims. Given the broad scope of the claims, the lack of guidance and working examples, the high level of unpredictability in the art, and the amount of experimentation, undue experimentation would be required for a skilled artisan to make the full scope of the claimed invention.

Claim Rejections - 35 USC § 103

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[12] The rejection of claims 107-108, 110-115, and 120-124 under 35 U.S.C. 103(a) as being unpatentable over Backman et al., Squirrell (1), Squirrell (2), and Gilles et al. is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action (5 May 2005 Office action at paragraph 18).

RESPONSE TO ARGUMENT: Applicant reiterates arguments from the prior response, arguing the examiner has combined the references through an inappropriate use of hindsight and attacking the reference of Backman et al., arguing Backman et al. does not teach luciferase production, does not require engineering of host cells to produce a mutant thermostable protein, and does not teach or suggest simultaneous production of a mutant thermostable protein and a mutant thermolabile protein. Thus, according to applicants, in view of these deficiencies, one of ordinary skill in the art would not combine the cited references with Backman et al.

Applicants' argument is not found persuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

At the time of the invention, the use of elevated temperature to purify luciferase from adenylate kinase activity was well-known in the art as evidenced by Squirrell et al.

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(1). As noted in the prior Office action, the reference of Squirrell et al. (1) suggests the use of elevated temperature to inactivate adenylate kinase activity in a preparation of luciferase. These teachings appear to be undisputed by applicants. However, while Squirrell et al. (1) clearly suggests the use of elevated temperature to inactivate adenylate kinase, the reference does not expressly teach inactivating a "thermosensitive" adenylate kinase in a preparation of a "thermostable" luciferase. The reference of Gilles et al. teaches an *E. coli* host cell that expresses an *E. coli* adenylate kinase that is inactivated at a temperature at which the luciferase of Squirrell et al. (2) remains active. Squirrell et al. (2) teaches *E. coli*-compatible vectors encoding a "thermostable" luciferase that remains active at a temperature at which the adenylate kinase of Gilles et al. is inactivated. Squirrell et al. (2) further teaches recombinant expression of the "thermostable" luciferase using *E. coli* as an expression host. Backman et al. teaches the concept of recombinantly expressing a "thermostable" protein followed by heat inactivation of a contaminating undesired protein that is a consequence of recombinant expression of the desired protein. These teachings appear to be undisputed by applicants. One of ordinary skill in the art, at the time of the invention would have used the *E. coli* host of Gilles et al. for recombinant production of the thermostable luciferase of Squirrell et al. (2) and then treated the resulting recombinant luciferase preparation at an "elevated ambient temperature" to inactivate the adenylate kinase activity as suggested by the methods of Squirrell et al. (1) and Backman et al.

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In this case, the examiner has not solely relied upon the teachings of Backman et al. in making the rejection. Instead, it is the combination of teachings, as summarized above and presented in greater detail in prior Office actions, that would have made the claimed invention obvious to one of ordinary skill in the art at the time of the invention. Applicants are reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

[13] The rejection of claims 117-119 and 125-127 under 35 U.S.C. 103(a) as being unpatentable over Backman et al. in view of Squirrell (1), Squirrell (2), and Gilles et al. as applied to claims 107-108, 110-115, and 120-124 above, and further in view of Novagen 1997 Catalog and Kiel et al. is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action (5 May 2005 Office action at paragraph 19).

RESPONSE TO ARGUMENT: Applicant reiterates arguments from the prior response, arguing the cited references would not motivate an ordinarily skilled artisan to make the claimed invention because, according to applicants, the references are non-analogous art.

Applicant's argument is not found persuasive. In response to applicant's argument that the cited references are nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be

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reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, all of the cited references pertain to the claimed invention. The reference of Backman et al. is concerned with heat inactivation of a thermosensitive contaminant protein in a preparation of a recombinant protein. Squirrell et al. (1) discusses adenylate kinase as a contaminating protein in a preparation of luciferase and the use of elevated temperature to remove adenylate kinase activity. Although applicants assert Squirrell et al. teaches thermosensitive luciferases, one of ordinary skill in the art would recognize that, by Squirrell et al. teaching that adenylate kinase activity can be inactivated in a preparation of luciferase by elevated temperature, the luciferase must necessarily be more thermostable than the adenylate kinase. Also, Squirrell et al. (2) clearly discloses "thermostable" luciferase polypeptides. Gilles et al. teaches an *E. coli* host that endogenously expresses a mutant temperature-sensitive adenylate kinase. Novagen 1997 Catalog teaches a system for recombinant production of proteins using *E. coli* as an expression host. Kiel et al. teaches a method for disrupting an endogenous gene in an *E. coli* cell that can be applied to the host as taught by Novagen 1997 Catalog. Clearly, one of ordinary skill in the art would recognize that all of the cited references are pertinent to the claimed invention and, for reasons of record, one of ordinary skill in the art would have been motivated to combine the cited references. As stated in the prior Office action, "[i]f applicant maintain their position that the references are non-

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analogous art, the examiner requests that applicants expressly state how the cited references are unrelated to applicant's endeavor or invention."

[14] The rejection of claims 107, 109-114, 116, and 128-132 under 35 U.S.C. 103(a) as being unpatentable over Backman et al. in view of Squirrell (1), Kajiyama et al., and Gilles et al. is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action (5 May 2005 Office action at paragraph 20).

RESPONSE TO ARGUMENT: Applicant argues Backman et al. fails to teach or suggest simultaneous production of a mutant protein with increased tolerance to a particular reaction condition and a mutant protein with decreased tolerance to the reaction condition. Thus, according to applicant, in view of this deficiency, one of ordinary skill in the art would not combine the reference of Gilles et al. with Backman et al. Applicant further argues the thermostable luciferase of Kajiyama et al. is not amendable to the "preferred" temperatures of Backman et al. Also, applicant argues that Squirrell et al. (1) does not cure the deficiencies of the combination of Backman et al., Kajiyama et al., and Gilles et al.

Applicants' argument is not found persuasive. That Backman et al. does not specifically teach that the undesired thermolabile contaminating protein is a mutant does not make the invention nonobvious. As noted above, it is the combination of references that would have made the invention obvious to one of ordinary skill in the art at the time of the invention. The reference of Squirrell et al. (1) suggests the use of an

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elevated temperature to inactivate adenylate kinase activity in a preparation of luciferase. This teaching appears to be undisputed by applicants. However, while Squirrell et al. (1) clearly suggests the use of elevated temperature to inactivate adenylate kinase, the reference does not expressly teach inactivating a “thermosensitive” adenylate kinase in a “thermostable” luciferase preparation. The reference of Gilles et al. teaches an *E. coli* host cell that expresses an adenylate kinase that is inactivated at a temperature at which the luciferase of Squirrell et al. (2) remains active. Squirrell et al. (2) teaches *E. coli*-compatible vectors encoding a “thermostable” luciferase that remains active at a temperature at which the adenylate kinase of Gilles et al. is inactivated. Backman et al. teaches a method of recombinantly expressing a “thermostable” protein followed by heat inactivation of a contaminating undesired protein that is a consequence of recombinant expression of the desired protein. These teachings appear to be undisputed by applicants. In this case, the examiner has not solely relied upon the teachings of Backman et al. in making the rejection. Instead, it is the combination of teachings, as summarized above, that would have made the claimed invention obvious to one of ordinary skill in the art at the time of the invention.

In response to applicant’s argument that the luciferase of Kajiyama et al. is not amendable to the “preferred” temperatures of the method of Backman et al., it is noted that a skilled artisan, in view of the teachings of Kajiyama et al., would have recognized that temperatures used in the *working example* would inactivate a luciferase polypeptide and would not have applied such relatively extreme temperatures in applying the concept of purifying a thermostable protein as disclosed by Backman et al. It should be

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noted that nowhere does Backman et al. teach that only extreme temperatures can be used in the practice of the disclosed method. Instead, the method of Backman et al. expressly teaches using a temperature that is "sufficient to inactivate said unwanted contaminants but not sufficient to inactivate said thermostable enzyme" (column 2).

In view of the *combined* teachings of Backman et al. in view of Squirrell (1), Kajiyama et al., and Gilles et al., the examiner maintains the position that the combination would have rendered the claimed invention obvious to one of ordinary skill in the art at the time of the invention.

[15] The rejection of claims 117-119 and 133-135 under 35 U.S.C. 103(a) as being unpatentable over Backman et al. in view of Squirrell (1), Kajiyama et al., and Gilles et al. as applied to claims 107, 109-114, 116, and 128-132 above, and further in view of Novagen 1997 Catalog and Kiel et al. is maintained for the reasons of record and the reasons stated above. The rejection was fully explained in a prior Office action (5 May 2005 Office action at paragraph 21).

RESPONSE TO ARGUMENT: Applicant argues the references of Novagen 1997 Catalog and Kiel et al. fail to cure the deficiencies of the other cited references.

Applicant's argument is not found persuasive. The alleged deficiencies have been addressed above. While a subcombination of the references, *i.e.*, a combination of fewer than all of the cited references, may not make the invention obvious, when one considers the combination of *all* of the cited references of Backman et al., Squirrell (1), Kajiyama et al., Gilles et al., Novagen 1997 Catalog and Kiel et al., it is the examiner's

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position that the claimed invention would have been obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

[16] Status of the claims:

Claims 107-135 are pending.

Claims 107-135 are rejected.

No claim is in condition for allowance.

All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


David J. Steadman, Ph.D.

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Primary Examiner
Art Unit 1656

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APPENDIX A

LOCUS 216516 107 aa linear 09-SEP-1993
 DEFINITION adenylate kinase.
 ACCESSION
 VERSION GI:216516
 DBSOURCE locus ECOADKVIS accession D90259
 KEYWORDS
 SOURCE Escherichia coli
 ORGANISM Escherichia coli
 Eubacteria; Proteobacteria; gamma subdivision; Enterobacteriaceae;
 Escherichia.
 REFERENCE 1 (residues 1 to 3576)
 AUTHORS Brune,M., Schumann,R. and Wittinghofer,F.
 TITLE Cloning and sequencing of the adenylate kinase gene (adk) of
 Escherichia coli
 JOURNAL Nucleic Acids Res. 13, 7139-7151 (1985)
 MEDLINE 86041903
 REFERENCE 2 (residues 1 to 3576)
 AUTHORS Miyamoto,K., Nakahigashi,K., Nishimura,K. and Inokuchi,H.
 TITLE Isolation and characterization of visible light-sensitive mutants
 of Escherichia coli K12
 JOURNAL J. Mol. Biol. 219, 393-398 (1991)
 MEDLINE 91269316
 REFERENCE 3 (residues 1 to 3576)
 AUTHORS Miyamoto,K.
 JOURNAL Unpublished (1993)
 COMMENT Submitted (07-DEC-1990) to DDBJ by: Kazumasa Miyamoto
 Dept. of Biophysics,
 Faculty of Science
 Kyoto University
 Sakyo-ku Kyoto
 Kyoto 606
 Japan
 Phone: 075-753-4200
 Fax: 075-791-0271.
 Method: conceptual translation.
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 adenosine monophosphates (AMP) and to yield adenosine
 diphosphates (ADP); cd01428"
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 ORIGIN
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 61 lveyhqmtap ligyyskeae agntkyakvd gtpkvaevra dlekilg